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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,949	02/20/2002	Stanley T. Crooke	ISIS-5027	8454

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EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/078,949	CROOKE, STANLEY T.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *165-201* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *165-173,175,179,180,184-193 and 197-199* is/are rejected.

7)☒ Claim(s) *174, 176-178, 181-183, 194-196, 200, 201* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/10/06 has been entered.

Applicant's arguments with respect to claims 165-201 have been considered but are moot in view of the new ground(s) of rejection. The new claims and applicants arguments set forth in the response filed 2/10/06 have overcome the rejection of record, but note the new grounds of rejection below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000.

Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 184-186, 190, 191, and 197-199 are rejected under 35 U.S.C. 102(e) as being anticipated by Goodchild et al [US 6,573,072].

The instantly rejected method is drawn to a method of detecting a double-stranded RNA nuclease in a sample where the **only method step** is the contacting of the sample with a double stranded RNA as described in the claims. It is noted that the claims require no more than the one method step. For example, there is no detection step and there is no requirement that there be any cleavage to be detected.

Goodchild et al disclose double stranded RNA compounds for administration to cells in a subject for treatment, including viral infection, for example (see columns 6-7). In Figure 1 it is disclosed a double stranded compound comprising an RNA ribozyme (R), an RNA substrate (S), and an RNA facilitator oligonucleotide (F4). F4 is a 13mer, S is a 33mer and R is a 35mer. All of these sizes are considered to be "about 17" or "about 20" since the specification does not provide any particular value to "about". In Example 2 (2) it has been disclosed an assay where a sample is contacted with the compound exemplified in Figure 1 where R contains 2'-O-methy modifications.

Claims 165-167, 172, 173, 179, 180, 184, 185, 190, 191, 197, and 198 are rejected under 35 U.S.C. 102(e) as being anticipated by Usman et al [US 6,849,726 B2].

The instantly rejected method of claims 184, 185, 190, 191, 197, and 198 is drawn to a method of detecting a double-stranded RNA nuclease in a sample where the **only method step** is the contacting of the sample with a double stranded RNA as described in the claims. It is noted that the claims require no more than the one method step. For example, there is no detection step and there is no requirement that there be any cleavage to be detected. The remainder of the claims are drawn to a method of activating a double stranded RNA nuclease.

Usman et al have disclosed Modified ribozymes that include abasicnucleotides, for example (see Example 5 and Figures 16-18). In example 8, the ribozyme of Figure 17 was administered to cell in culture where the ribozyme hybridized and cleaved its substrate (an RNA) the instant example meets all the limitations of the rejected claims since the double stranded RNA was brought into contact with an RNA nuclease by virtue if being administered to cells that would contain a double stranded RNA nuclease. The double stranded RNA meets all of the structural limitation required in the claims. Without the ability to test the compounds of the prior art, the examiner shifts the burden to applicant to demonstrate that the double stranded RNA disclosed in Usman et al would not activate a double-stranded RNA nuclease.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 189, 192 and 193 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodchild et al [US 6,573,072].

The instantly rejected method is drawn to a method of detecting a double-stranded RNA nuclease in a sample where the **only method step** is the contacting of the sample with a double stranded RNA as described in the claims. It is noted that the claims require no more than the one method step. For example, there is no detection step and there is no requirement that there be any cleavage to be detected.

Goodchild et al disclose double stranded RNA compounds for administration to cells in a subject for treatment, including viral infection, for example (see columns 6-7). In Figure 1 it is disclosed a double stranded compound comprising an RNA ribozyme (R), an RNA substrate (S), and an RNA facilitator oligonucleotide (F4). F4 is a 13mer, S is a 33mer and R is a 35mer. All of these sizes are considered to be "about 17" or "about 20" since the specification does not provide any particular value to "about". In Example 2 (2) it has been disclosed an assay where a sample is contacted with the compound exemplified in Figure 1 where R contains 2'-O-methy modifications.

Example 2(2) does not specifically disclose the use of phosphorothioate linkages in one, the other or both of a first and second oligonucleotide. However Goodchild et al have clearly taught that the facilitator oligonucleotide and ribozymes can be modified to

increase resistance to degradation (columns 6-7) which teaching includes phosphorothioate modifications. One in the art would clearly have been motivated to modify the facilitator and/or ribozymes of the invention to include phosphorothioate modifications since it was expressly suggested to do so.

The invention as a whole would therefore have been prima facie obvious to one in the art at the time the invention was made.

Claims 187 and 188 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodchild et al [US 6,573,072] in view of Uhlmann et al [US 6,037,463].

The instantly rejected method is drawn to a method of detecting a double-stranded RNA nuclease in a sample where the **only method step** is the contacting of the sample with a double stranded RNA as described in the claims. It is noted that the claims require no more than the one method step. For example, there is no detection step and there is no requirement that there be any cleavage to be detected.

Goodchild et al disclose double stranded RNA compounds for administration to cells in a subject for treatment, including viral infection, for example (see columns 6-7). In Figure 1 it is disclosed a double stranded compound comprising an RNA ribozyme (R), an RNA substrate (S), and an RNA facilitator oligonucleotide (F4). F4 is a 13mer, S is a 33mer and R is a 35mer. All of these sizes are considered to be "about 17" or "about 20" since the specification does not provide any particular value to "about". In

Example 2 (2) it has been disclosed an assay where a sample is contacted with the compound exemplified in Figure 1 where R contains 2'-O-methy modifications.

Goodchild et al do not specifically teach the use of 2' modifications fluoro and 2'-O-methoxyethyl. However Uhlmann et al have taught that such 2' modifications where known and routinely used in the art at the time of invention at paragraphs 10-12 and in claims 6, 7, 11, 12, and 18, for example.

The invention as a whole would therefore have been prima facie obvious to one in the art at the time the invention was made.

Claims 165-169, 171-173, 175, 179, 180, 184-187, 189-191, 193, 197, and 198 rejected under 35 U.S.C. 103(a) as being unpatentable over Usman et al [US 6,849,726].

The claimed invention is drawn to the activation of a double stranded RNA nuclease via the "contacting" of the nuclease with a double stranded RNA. The instantly Claimed invention is also drawn to a method of detecting a double-stranded RNA nuclease in a sample where the **only method step** is the contacting of the sample with a double stranded RNA as described in the claims. It is noted that the claims require no more than the one method step. For example, there is no detection step and there is no requirement that there be any cleavage to be detected.

Usman et al have taught the targeting of RNA via modified ribozymes. A target RNA hybridized by a ribozyme targeting it is a double stranded RNA. A double stranded

ribozyme/ target RNA in a cell is "contacted" with any double stranded RNA nucleases within that cell. The ribozymes of Usman are taught to be modified with various sugar, base and backbone modifications or combinations thereof (see claim 3 for example). In claims 7 and 10 it is taught 2'-O methyl and 2'-Fluoro modifications. In claims 8 and 11 it has been taught phosphorothioate modifications, for example. In Figures 16 and 17, for example, one can clearly see that based on the teachings of Usman et al the ribozymes of their invention can contain 8 consecutive 2'-hydroxyl ribonucleosides with phosphodiester linkages. One would know based on the teachings of Usman et al that the 2'hydroxy residues can be phosphodiester by simply referring to Figures 16 and 17, for example. In regard to claim 175 it is noted that Usman et al have taught that the ribozyme can be modified to contain phosphorothioate linkages and the target RNA would be phosphodiester when an mRNA is targeted, for example. The claimed invention is obvious in view of the fact that the claimed method requires only one step of contacting a double stranded RNA nuclease with a double stranded RNA. It is noted that the double stranded RNA of Usman et al {a modified ribozyme hybridized to its target] meets all of the structural limitations of the claimed invention and based on the teachings of Usman one would clearly be motivated to contact cells with the Ribozymes they teach since they are designed for inhibiting disease related mRNA targets, for example. One would make the instantly recited modifications to the ribozymes of Usman et al since Usman et al specifically suggest doing so.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Claims 170 and 188 are rejected under 35 U.S.C. 103(a) as being unpatentable over Usman et al [US 6,849,726] as applied above in view of Uhlmann et al [US 6,037,463].

The claimed invention is as described above with the added limitation of the double stranded RNA containing a 2'-O-methoxyethyl modification.

Usman et al is relied on as above. Usman et al do not specifically teach a 2'-O-methoxyethyl modification. . However Uhlmann et al have taught that such 2' modifications where known and routinely used in the art at the time of invention at paragraphs 10-12 and in claims 6, 7, 11, 12, and 18, for example.

It would have been routine to select such a 2' modification especially in view of the fact that Usman et al have taught the use of 2'-O modifications in general where the specifically recited modification is within the scope of that described by Usman et al and is used for the same purposes as those modifications specifically taught by Usman et al and where the specific modification is taught by Uhlman for the same purposes.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Claims 174, 176-178, 181-183, 194-196, 200 and 201 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sean R McGarry
Primary Examiner
Art Unit 1635